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Cutaneous histoplasmosis. A case report

Authors: Galo G. Farfán-Cano[1,2,3,4,*], Stanley G. Farfán-Cano[1,2,3], Harold R. Farfán-Cano[3], Glen A. Silva-Rojas[4], Maria T. Solórzano-Bravo[1,2,3,4,6]

[1]Society of Infectious Diseases of Guayas (SIG), Guayaquil, Ecuador.
[2]King Juan Carlos University, Madrid, España.
[3]University of Guayaquil, Guayaquil, Ecuador.
[4]Northern of Guayaquil Los Ceibos General Hospital, Guayaquil, Ecuador.
[5]Catholic University of Santiago de Guayaquil, Guayaquil, Ecuador.
[6]Pontifical Catholic University of Argentina, Buenos Aires, Argentina.
[*]https://orcid.org/0000-0001-8447-5764

Corresponding author:
Galo Guillermo Farfán Cano (Main Author)
Address: Kennedy Este (Guayaquil - Ecuador), phone: +593 98 499 6856.
E-mail: dr.galo.farfan.cano@gmail.com

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Abstract

Histoplasmosis is an endemic infection of Ecuador, its forms of presentation can be varied and florid, especially in immunosuppressed patients, its lethality is high, hence its diagnosis and treatment should be based on both clinical and laboratory results. Cutaneous histoplasmosis is a form of disseminated *Histoplasma capsulatum* infection rarely described in HIV patients. The following is a description of the diagnosis and treatment of a patient with generalized papular skin lesions, heat stroke, diarrhea, attributed to adverse reaction of gastritis treatment of 10 days of evolution, this was associated with a recent diagnosis of HIV infection following his admission to hospital.

Key word: histoplasma capsulatum infection, aids-related opportunistic infections, histoplasmosis, cutaneous histoplasmosis, HIV.

Introduction

Histoplasmosis is a systemic mycosis considered endemic in Ecuador and in the rest of the countries of the Americas, with a wide geographical distribution and reported in the 5 continents, it is considered one of the opportunistic diseases markers of stage C3 of acquired immunodeficiency syndrome AIDS (1).

The etiological agent is the dimorphic fungus (which can present under two morphological aspects) *Histoplasma capsulatum* var. *capsulatum* in most cases, although other varieties have been described, such as var. *duboisii*, var. *farciminosum*, which tends to be found in soils rich in organic material with bird or bat feces, and the entrance route to the human organism is through the inhalation of microconidia. It usually grows as yeast at 35°C, which is the pathogenic form found in infected tissues (1,2).

In the disseminated form the most common symptoms are usually fever, night sweats and cough, characteristic of "respiratory symptomatic" patients, and therefore must be differentiated from tuberculosis, it is also usually accompanied by weight loss, fatigue, abdominal pain or diarrhea; the presence of mucocutaneous lesions is important for the differentiation of tuberculosis, but should not be considered pathognomonic, especially in view of the likelihood of Hansen's disease (3–7).

A search using mesh terms and Boolean operator (Cutaneous histoplasmosis) AND (AIDS-Related Opportunistic Infections) yielded 7 results in the last 5 years at march 30 of 2022, which led us to update the bibliography after reviewing the instructions for authors, highlighting the rarity of cases of cutaneous histoplasmosis among immunosuppressed patients in the context of HIV infection.

Case report

22-year-old male patient, heterosexually oriented, who during questioning refers to high risk sexual behavior (multiple sexual partners), with occasional use of condoms, frequent alcohol consumption, denying use of recreational drugs or narcotics, he didn't refer any exposure to bird or bat feces.

The patient's clinical condition was characterized by high fever, diffuse abdominal pain and liquid stools (6 times a day) for 10 days, accompanied by papular nodular skin lesions on the forehead, cheeks, peribuccal area and chin, which were associated with the patient taking amoxicillin/clavulanate and clarithromycin prescribed due to a positive stool test for Helicobacter pylori.

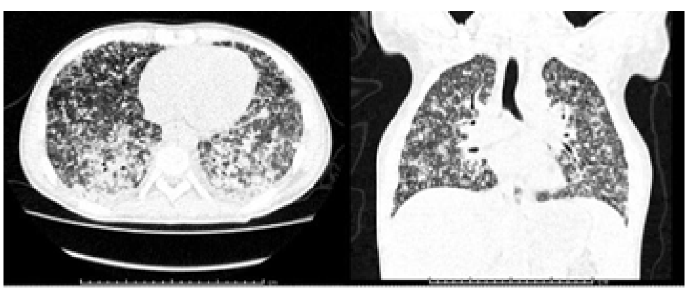
On admission, the patient was normal-headed, with papulo-nodular lesions, with a vesicular appearance in the face, palpable cervical lymphadenopathy, additionally to the cutaneous lesions, were founded symmetrical thorax with rales in both pulmonary fields, rhythmic heart sounds, no respiratory symptoms; soft abdomen, depressible, with tympanism, increased bowel sounds, no megalys, no inguinal adenopathies, symmetrical extremities without edema.

Because of the patient's acute condition, complementary radiographic and laboratory tests were requested, with reactive results for HIV in fourth-generation immunochromatography, with results of 118.7 and 107 COI in third-generation electrochemical-luminescence tests for two different samples. Chest radiography (Figure 1) showed a diffuse miliary-looking alveolar condensation pattern. Because of the radiographic image, a chest tomography was requested (Figure 2), in which a septal thickening was observed, an interstitial-alveolar pattern predominant in both lung bases, with a micronodular pattern in vertices and midfields. ELISA Hepatitis B, C, and A results were negative, lymphopenia <0.4 x103 U/L, and serum creatinine 0.75 mg/dl at the time of admission.

Figure 1
Chest X-ray showing miliary pattern



Figure 2
Chest tomography with interstitial-alveolar and micronodular patterns



With the results of reactive tests for HIV, a specialist evaluation was requested for infectious diseases, dermatology evaluation to take a skin tissue biopsy for microbiological and anatomopathological assessments of skin lesions (Figure 3), pneumology evaluation to perform bronchial lavage with microbiological studies, antigen detection for Cryptosporidium in feces and coproculture.

Figure 3
On admission´s photograph: Papular and nodular lesions on the patient's face, before the start of treatment; the globular aspect of the lesions is striking



Besides, treatment with amphotericin B deoxycholate at a dose of 0.5 mg/kg intravenously every 24 hours was started empirically, together with anti-tuberculosis treatment with rifampicin, pyrazinamide, ethambutol, and isoniazid, as well as prophylaxis for P. *jirovecii* with TMP/SMX 800/160 mg each day.

The skin biopsy was performed 24 hours after starting the empirical antimicrobial scheme, while bronchial lavage sampling was performed on the 7th day of treatment. No bacterial growth, fungal structures or yeasts were observed in the bronchial lavage cultures until 48 hours after incubation. Also, the Ziehl-Neelsen stain was negative. No bacterial growth was evident in the results of blood and urine cultures. The coproculture was negative for the development of enteropathogens, no fungal structures or yeasts were evident, Ziehl-Neelsen staining (modified in feces) was negative, the stool testing revealed the presence of cysts of Blastocystis hominis, the detection of Cryptosporidium parvum antigen was negative.

Yeast-form of Histoplasma capsulatum was isolated from skin obtained from the papular lesions from culture of tissue as well as from the anatomopathological samples.

Figure 4
Yeast-form of Histoplasma capsulatum isolated from skin biopsy culture of facial lesions, with Wright's stain (Miguel Merejildo, Lic. of clinical laboratory)

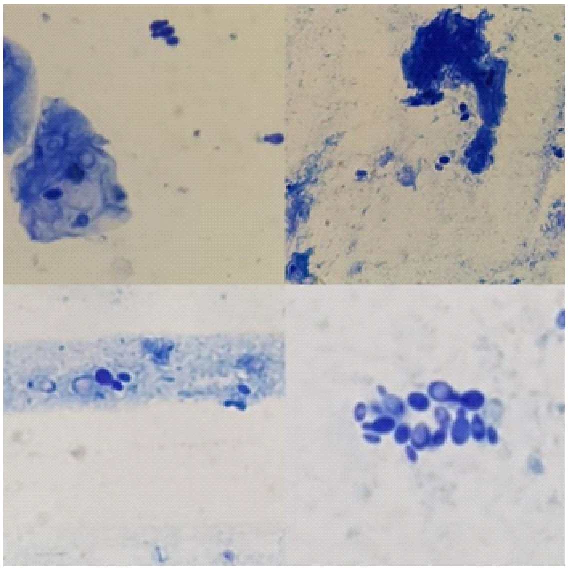
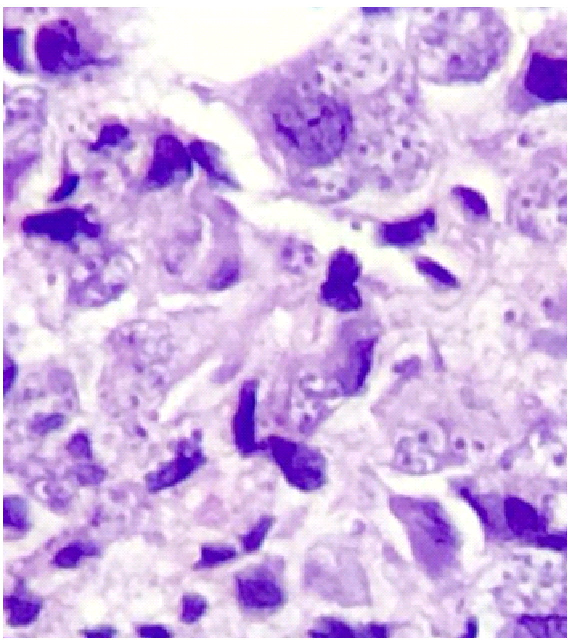


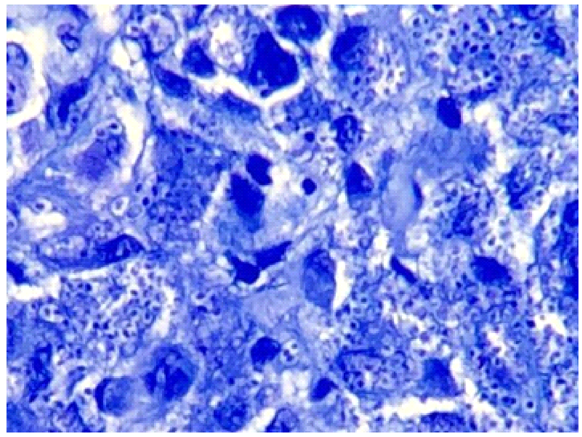
Figure 5
Yeasts are observed inside the histiocytes compatible with yeast of Histoplasma capsulatum with Hematoxylin/Eosin staining. (Andrea Hinojosa and Daysi Perón, Specialists in Pathological Anatomy)



HIV viral load was 377,000 copies and T lymphocytes CD 4 was 12 cells/mm3. After 10 days of treatment, papular lesions covered with scabs in the involution process, and lower limb edema, associated with treatment with amphotericin B deoxycholate was evidenced.

With the results of viral load and T lymphocytes CD4, skin biopsy and previous cultures negative, with preserved renal function, with a serum creatinine value of 0.49 mg/dL, and a sustained lymphopenia of 0.50 x103 U/L, transaminases values above 70 for AST (69-65 IU, with tendency to decrease) and sustained in the case of ALT (37 IU), and LDH with value of 238 IU, 3 days after the beginning of the antimicrobial scheme and amphotericin the patient was reevaluated by the infectious disease unit, with these laboratory results and lower limb edema, absence of fever and absence of signs and symptoms of respiratory distress, it was indicated to change the antifungal scheme and start itraconazole 200 mg orally every 8 hours during the first 3 days, from the 4th day onwards maintaining itraconazole 200 mg orally every 12 hours for at least 12 month, as well as maintaining the antifungal scheme and prophylaxis for PCP.

Figure 6
Intracellular yeasts are observed in Giemsa staining (Andrea Hinojosa and Daysi Perón, Specialists in Pathological Anatomy)



After 15 days of hospitalization, the patient was discharged without edema in his extremities, with his hepatic and renal function preserved, and with slow but favorable involution of the dermal lesions.

Ethical aspects: informed consent was obtained for the use of images and results for the patient's written case report. Authorization was given to the sub-directorate of teaching and research to collect the information from the clinical history.

Discussion

Histoplasmosis is a systemic infection considered as opportunistic in patients with immunosuppression, it commonly affects patients with AIDS around the world, it´s prevalence is considered high, particularly in the regions of North America and Latin America, where infections by H. *capsulatum* var. *capsulatum* are predominant (1,2,5,8–10).

The increase in immunocompromised patients after the HIV pandemic has produced an increase in the number of cases of disseminated histoplasmosis, which is estimated to be under-diagnosed due to the lack of availability of diagnostic tests, as well as the lack of consideration of histoplasmosis as the main cause of infection (especially due to its similarity to miliary tuberculosis, with which it can often coexist) (10–12). In the study by Da Silva et al. the predominance of disease was male (3.6 to 1 ratio) and 41% of patients were diagnosed with HIV and Histoplasmosis simultaneously, with cutaneous presentation being the least frequent form (10).

In Brazil, a frequency of 8.9 - 89% positive for histoplasma skin tests was indicated between 1975 and 2010, being more frequent in the southern and mid-eastern states and an estimated incidence of 2.19 cases per 1000 hospital admissions, with 255 cases reported by 2011 while in Venezuela 663 cases were reported between 1984 and 2010, It is not unusual for histoplasmosis to be identified as a serious contributor to AIDS-related mortality (13).

Tissue, fluid or blood cultures are utilized for the detection of micro-organisms and definitive diagnosis, as well as pathological anatomical studies (2,5,8,12–14).

The first-line agent for treatment of Histoplasmosis is different forms of presentation of amphotericin B (dose of 3.0 - 5 mg/kg day, for 1 to 2 weeks in the case of liposomal amphotericin), the liposomal presentation is preferable due to decreased renal toxicity and evidence of superior efficacy over the other presentations, however, that does not disqualify the deoxycholate amphotericin B (0.3 - 1 mg/kg day, for 7 to 15 days) as a first-line therapy, by endogenous route (2,4,5,8). However, poor response to amphotericin B deoxycholate has been reported both because of the clinical conditions of the patients, as well as the toxicity of this drug formulation (10).

Conclusions

Histoplasma capsulatum is a dimorphic fungus considered endemic in Ecuador and other countries of America. Histoplasmosis is an opportunistic infection that especially affects AIDS patients with a count of CD4 of 200 cells/mm^3 or less.

The diagnosis of histoplasmosis can be made by traditional culture methods; however, this still has the disadvantage of an incubation time of 21 days on average. Currently, there are antigen-based diagnostic methods for H. *capsulatum*, as well as those based on antibodies and DNA that allow a rapid diagnosis, resulting in timely treatment and clinical improvement of the patient, with the limitation of their accessibility due to their cost in such countries as Ecuador.

First-line treatment for Histoplasmosis is liposomal amphotericin B, and deoxycholate as an alternative. Itraconazole is used as subsequent treatment for amphotericin B when the need for ventilatory support and/or fever dissipates, its use is recommended for at least 12 months.

Funding

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Conflicts of Interest

All authors declare no conflict of interest for this article.

Ethics

For the presentation of this clinical case, we had the approval and informed consent of the patient and the sub-directorate of teaching of the Hospital.

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